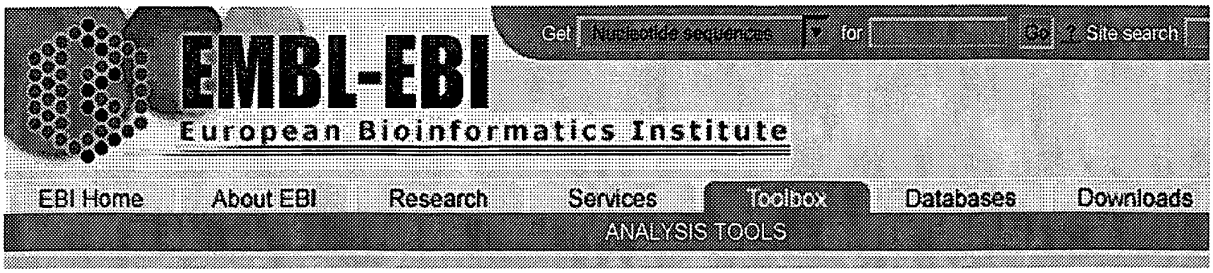

EBI Generic DB Entry Retrieval

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SV   L35496.1
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DT   23-AUG-1994 (Rel. 40, Created)
DT   04-MAR-2000 (Rel. 63, Last updated, Version 3)
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DE   Clostridium botulinum proteolytic type F neurotoxin bonT/F gene, complete
DE   cds, and nontoxic-nonhaemagglutinin (ntnH) gene, 3' end.
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KW   bonT/F gene; neurotoxin type F; nontoxic-nonhaemagglutinin; ntnH gene.
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OS   Clostridium botulinum
OC   Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae;
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RA   Elmore M.J., Bodsworth N.J., Whelan S.M., Minton N.P.;
RT   "The complete nucleotide sequence of the gene coding for proteolytic type
RT   neurotoxin of Clostridium botulinum";
RL   Unpublished.
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L1 ANSWER 13 OF 17 MEDLINE
AN 97016817 MEDLINE
DN 97016817 PubMed ID: 8863443
TI Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic Clostridium botulinum types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.
AU East A K; Bhandari M; Stacey J M; Campbell K D; Collins M D
CS Department of Microbiology, Institute of Food Research, Reading, Berkshire, United Kingdom.. alison.east@bbsrc.ac.uk
SO INTERNATIONAL JOURNAL OF SYSTEMATIC BACTERIOLOGY, (1996 Oct) 46 (4) 1105-12.
Journal code: 0042143. ISSN: 0020-7713.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X78230; GENBANK-X87974; GENBANK-X92973; GENBANK-X96491; GENBANK-X96492; GENBANK-X96493; GENBANK-X96494
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961115
AB The cluster of genes encoding components of the **botulinum neurotoxin** (BoNT) complex was mapped in proteolytic (group I) Clostridium botulinum strains encoding BoNT types A, B, and F. Two different arrangements of genes were found: type A strain 62A and type B strain NCTC 7273 have similar organizations of genes encoding BoNT, the nontoxic nonhemagglutinin component (NTNH), hemagglutinin components, and P-21; **type F** strain Langeland has genes encoding BoNT, NTNH, and P-21, and a previously unidentified open reading frame encoding a protein of 416 amino acids. A group of type A strains typified by infant strain Kyoto-F, which is unlike type A strain 62A, lacks genes for hemagglutinin components and exhibits an organization similar to that of **type F**. Sequencing and pairwise analysis revealed the presence of possible chimeric sequences in some NTNH genes of proteolytic C. botulinum. Discordance in genealogical trees derived from different regions of the NTNH genes was observed which could be symptomatic of recombination and which may indicate that the NTNH gene represents a hot spot for such events within the cluster of genes encoding the BoNT complex. It is also evident that the phylogenetics of the NTNH gene, which is linked to the gene encoding BoNT, does not mirror the evolutionary history of the BoNT, upon which the C. botulinum species complex is defined and subdivided.

L1 ANSWER 14 OF 17 MEDLINE
AN 94297488 MEDLINE
DN 94297488 PubMed ID: 7764998
TI Conserved structure of genes encoding components of **botulinum neurotoxin** complex M and the sequence of the gene coding for the nontoxic component in nonproteolytic Clostridium botulinum **type F**.
AU East A K; Collins M D
CS Department of Microbiology, Institute of Food Research, Reading Laboratory, UK.
SO CURRENT MICROBIOLOGY, (1994 Aug) 29 (2) 69-77.
Journal code: 7808448. ISSN: 0343-8651.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Biotechnology
EM 199408

ED Entered STN: 19950809
Last Updated on STN: 19970203
Entered Medline: 19940810

AB For investigation of the genes of proteins associated in vivo with **botulinum neurotoxin** (BoNT), polymerase chain reaction (PCR) experiments were carried out with oligonucleotide primers designed to regions of the nontoxic-nonhemagglutinin (NTNH) gene of Clostridium botulinum type C. The primers were used to amplify a DNA fragment from genomic DNA of C. botulinum types A, B, E, F, G and toxigenic strains of Clostridium barati and Clostridium butyricum. The amplified product from all of these strains hybridized with an internal oligonucleotide probe, whereas all nontoxigenic clostridia tested gave no PCR product and showed no reaction with the probe. The NTNH gene was shown to be located upstream of the gene encoding BoNT, thereby revealing a conserved structure for genes encoding the proteins of the M complex of the progenitor botulinum toxin in these organisms. The sequence of the NTNH gene of nonproteolytic C. botulinum **type F** was determined by PCR amplification and sequencing of overlapping cloned fragments. NTNH/F showed 71% and 61% identity with NTNH of C. botulinum type E and type C respectively.

L1 ANSWER 15 OF 17 MEDLINE
AN 93012902 MEDLINE
DN 93012902 PubMed ID: 1398040
TI Sequence of the gene encoding **type F** neurotoxin of Clostridium botulinum.
AU East A K; Richardson P T; Allaway D; Collins M D; Roberts T A; Thompson D E
CS Department of Microbiology, AFRC Institute of Food Research, Reading, UK.
SO FEMS MICROBIOLOGY LETTERS, (1992 Sep 15) 75 (2-3) 225-30.
Journal code: 7705721. ISSN: 0378-1097.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M92906
EM 199211
ED Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921119

AB Primers designed to conserved regions of botulinum and tetanus clostridial toxins were used to amplify DNA fragments from non-proteolytic Clostridium botulinum **type F** (202F) DNA using polymerase chain reaction technology. The fragments were cloned and the complete nucleotide sequence of the gene encoding **type F** toxin determined. Analysis of the nucleotide sequence demonstrated the presence of an open frame encoding a protein of 1274 amino acids, similar to other **botulinum neurotoxins**. Upstream of the toxin gene is the end of an open reading frame which encodes the C-terminus of a protein with homology to non-toxic-non-hemagglutinin component of type C progenitor toxin.

L1 ANSWER 16 OF 17 MEDLINE
AN 90262533 MEDLINE
DN 90262533 PubMed ID: 2188647
TI Botulinum **type F** neurotoxin. Large-scale purification and characterization of its binding to rat cerebrocortical synaptosomes.
AU Wadsworth J D; Desai M; Tranter H S; King H J; Hambleton P; Melling J; Dolly J O; Shone C C
CS Department of Biochemistry, Imperial College of Science and Technology, London, U.K.
SO BIOCHEMICAL JOURNAL, (1990 May 15) 268 (1) 123-8.

[redacted]

Journal code: 2984726R. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199006
ED Entered STN: 19900720
Last Updated on STN: 19970203
Entered Medline: 19900628
AB 1. A large-scale purification procedure has been developed for Clostridium botulinum **type F** neurotoxin. Commencing with 160 litres of bacterial culture, 101 mg of purified **type F** neurotoxin with a specific toxicity of 2 x 10(7) mouse LD50 (median lethal dose).mg-1 were obtained. 2. Purified **type F** neurotoxin was labelled to high specific radioactivity (900-1360 Ci/mmol) without loss of biological activity using a chloramine-T procedure. Of the two neurotoxin subunits, the heavy chain was preferentially radiolabelled. 3. Radiolabelled **type F** neurotoxin displayed specific saturable binding to rat synaptosomes. At least two pools of acceptors were evident: a low content of high-affinity acceptors sites [KD approximately 0.15 nM; Bmax (maximal binding) 20 fmol/mg] and a larger pool of lower-affinity sites (KD greater than 20 nM; Bmax greater than 700 fmol/mg). Both pools of acceptors were sensitive to trypsin and neuraminidase treatment, which suggests that protein and sialic acid residues are components of the synaptosomal acceptors. 4. Experiments investigating competition among **botulinum neurotoxin** types A, B, E and F for acceptors on rat brain synaptosomes showed that **type F** neurotoxin binds to acceptor molecules which are completely distinct from those of the other three neurotoxins.

L1 ANSWER 17 OF 17 MEDLINE
AN 84018414 MEDLINE
DN 84018414 PubMed ID: 6353671
TI Amino acid composition of Clostridium botulinum **type F** neurotoxin.
AU DasGupta B E; Rasmussen S
NC NS 17742 (NINDS)
SO TOXICON, (1983) 21 (4) 566-9.
Journal code: 1307333. ISSN: 0041-0101.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198311
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19831123
AB To develop reliable data on the amino acid composition of **type F botulinum neurotoxin**, three batches of the neurotoxin were analyzed. Each batch was isolated from a separate neurotoxin producing bacterial culture. Two batches had inoculum from one source and the other batch one from a different source. Two batches of the neurotoxin were purified by the same method and one was purified by a different method. The neurotoxin preparations were found comparable in purity and similar in amino acid composition. The best estimate of number of amino acid residues per neurotoxin molecule (mol. wt. 155,000) was: Asp218 Thr80 Ser105 Glu128 Pro47 Gly69 Ala47 Val72 CyS9 Met14 Ile128 Leu104 Tyr86 Phe60 Lys90 His13 Arg51 Trp23.

=>

L2 ANSWER 7 OF 10 MEDLINE
AN 95179082 MEDLINE
DN 95179082 PubMed ID: 7874084
TI Inhibition of neurotransmitter release by clostridial neurotoxins correlates with specific proteolysis of synaptosomal proteins.
AU Blasi J; Binz T; Yamasaki S; Link E; Niemann H; Jahn R
CS Departament de Biologia Cel.lular i Anatomia Patologica, Facultat de Medicina, Universitat de Barcelona, Spain.
SO JOURNAL OF PHYSIOLOGY, PARIS, (1994) 88 (4) 235-41.
Journal code: 9309351. ISSN: 0928-4257.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19970203
Entered Medline: 19950404
AB Rat brain synaptosomes were used to study the effect of several clostridial neurotoxins on the neurotransmitter release. In this system the blockade of transmitter release correlated with the proteolytic activity of the toxins. Blockade of glutamate release was linked to selective proteolysis of one of the following synaptic proteins: synaptobrevin (BoNT/D, **BoNT/F**); SNAP-25 (BoNT/A, BoNT/E), or HPC-1/syntaxin (BoNT/C1). All the toxins used had an inhibitory effect on synaptosomes with the exception of **BoNT/F**. **BoNT/F** cleaved synaptobrevin in permeabilized synaptosomes but failed to produce the same effect on intact synaptosomes.

L2 ANSWER 8 OF 10 MEDLINE
AN 94230352 MEDLINE
DN 94230352 PubMed ID: 8175689
TI Cleavage of members of the synaptobrevin/VAMP family by types D and F botulinal neurotoxins and tetanus toxin.
AU Yamasaki S; Baumeister A; Binz T; Blasi J; Link E; Cornille F; Roques B; Fykse E M; Sudhof T C; Jahn R; +
CS Department of Microbiology, Federal Research Center for Virus Diseases of Animals, Tubingen, Federal Republic of Germany.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Apr 29) 269 (17) 12764-72.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940620
Last Updated on STN: 19970203
Entered Medline: 19940606
AB Tetanus toxin (TeTx) and the various forms of botulinal neurotoxins (BoNT/A to BoNT/G) potently inhibit neurotransmission by means of their L chains which selectively proteolyze synaptic proteins such as synaptobrevin (TeTx, BoNT/B, **BoNT/F**), SNAP-25 (BoNT/A), and syntaxin (BoNT/C1). Here we show that BoNT/D cleaves rat synaptobrevin 1 and 2 in toxified synaptosomes and in isolated vesicles. In contrast, synaptobrevin 1, as generated by in vitro translation, is only a poor substrate for BoNT/D, whereas this species is cleaved by **BoNT/F** with similar potency. Cleavage by BoNT/D occurs at the peptide bond Lys59-Leu60 which is adjacent to the **BoNT/F** cleavage site (Gln58-Lys59) and again differs from the site hydrolyzed by TeTx and BoNT/B (Gln76-Phe77). Cellubrevin, a recently

discovered isoform expressed outside the nervous system, is efficiently cleaved by all three toxins examined. For further characterization of the substrate requirements of BoNT/D, we tested amino- and carboxyl-terminal deletion mutants of synaptobrevin 2 as well as synthetic peptides. Shorter peptides containing up to 15 amino acids on either side of the cleavage site were not cleaved, and a peptide extending from Arg47 to Thr116 was a poor substrate for all three toxins tested. However, cleavability was restored when the peptide is further extended at the NH2 terminus (Thr27-Thr116) demonstrating that NH2 terminally located sequences of synaptobrevin which are distal from the respective cleavage sites are required for proteolysis. To further examine the isoform specificity, several mutants of rat synaptobrevin 2 were generated in which individual amino acids were replaced with those found in rat synaptobrevin 1. We show that a Met46 to Ile46 substitution drastically diminishes cleavability by BoNT/D and that the presence of Val76 instead of Gln76 dictates the reduced cleavability of synaptobrevin isoforms by TeTx.

L2 ANSWER 9 OF 10 MEDLINE
AN 94013372 MEDLINE
DN 94013372 PubMed ID: 8408542
TI Gene probes for identification of the botulinal neurotoxin gene and specific identification of neurotoxin types B, E, and F.
AU Campbell K D; Collins M D; East A K
CS Reading Laboratory, Institute of Food Research, Agriculture and Food Research Council, United Kingdom.
SO JOURNAL OF CLINICAL MICROBIOLOGY, (1993 Sep) 31 (9) 2255-62.
Journal code: 7505564. ISSN: 0095-1137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X70814; GENBANK-X70815; GENBANK-X70816; GENBANK-X70817; GENBANK-X70818; GENBANK-X70819; GENBANK-X70820; GENBANK-X70821
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931102
AB A polymerase chain reaction method was developed for the specific detection of the botulinum neurotoxin (BoNT) gene of Clostridium botulinum. Degenerate oligonucleotide primers, designed from the nucleotide sequence of the heavy chain of the BoNT gene, amplified a specific fragment of approximately 1.1 kb from strains of C. botulinum toxin types A, B, E, F, and G and neurotoxin-producing strains of Clostridium barati and Clostridium butyricum, but no fragment was obtained from nontoxigenic strains. The fragments amplified from several strains of C. botulinum types B, E, and F were cloned in Escherichia coli and their nucleotide sequences were determined. Sequences within this region were used to design oligonucleotide probes specific for BoNT type B (BoNT/B), BoNT/E, and **BoNT/F** genes. An additional probe was designed for the detection of the **BoNT/F** gene of C. barati, which differed in sequence from **BoNT/F** genes of both proteolytic and nonproteolytic strains of C. botulinum.

L2 ANSWER 10 OF 10 MEDLINE
AN 93012902 MEDLINE
DN 93012902 PubMed ID: 1398040
TI Sequence of the gene encoding type F neurotoxin of Clostridium botulinum.
AU East A K; Richardson P T; Allaway D; Collins M D; Roberts T A; Thompson D E
CS Department of Microbiology, AFRC Institute of Food Research, Reading, UK.
SO FEMS MICROBIOLOGY LETTERS, (1992 Sep 15) 75 (2-3) 225-30.
Journal code: 7705721. ISSN: 0378-1097.

[redacted]

CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M92906
EM 199211
ED Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921119
AB Primers designed to conserved regions of botulinum and tetanus clostridial toxins were used to amplify DNA fragments from non-proteolytic Clostridium botulinum type F (202F) DNA using polymerase chain reaction technology. The fragments were cloned and the complete nucleotide sequence of the gene encoding type F toxin determined. Analysis of the nucleotide sequence demonstrated the presence of an open frame encoding a protein of 1274 amino acids, similar to other botulinum neurotoxins. Upstream of the toxin gene is the end of an open reading frame which encodes the C-terminus of a protein with homology to non-toxic-non-hemagglutinin component of type C progenitor toxin.

=>

1: P10845. Botulinum neuroto...[gi:399133] Links

```
LOCUS       BXA1_CLOBO              1296 aa            linear   BCT 15-JUN-2002
DEFINITION  Botulinum neurotoxin type A precursor (BoNT/A) (Bontoxilysin A)
            (BOTOX) [Contains: Botulinum neurotoxin A, light-chain; Botulinum
            neurotoxin A, heavy-chain].
ACCESSION   P10845
VERSION     P10845  GI:399133
DBSOURCE    swissprot: locus BXA1_CLOBO, accession P10845;
            class: standard.
            extra accessions:P18639,P01561,created: Jul 1, 1989.
            sequence updated: Jul 1, 1993.
            annotation updated: Jun 15, 2002.
            xrefs: gi: 40381, gi: 40382, gi: 144864, gi: 144865, gi: 1619251,
            gi: 1619253, gi: 2160224, gi: 2160225, gi: 144880, gi: 551776, gi:
            279630, gi: 98562, pdb accession 3BTA
            xrefs (non-sequence databases): MEROPS M27.002, InterPro IPR000395,
            InterPro IPR000130, Pfam PF01742, PRINTS PR00760, ProDom PD001963,
            PROSITE PS00142
KEYWORDS    Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc;
            Pharmaceutical; 3D-structure.
SOURCE      Clostridium botulinum.
  ORGANISM  Clostridium botulinum
            Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae;
            Clostridium.
REFERENCE   1  (residues 1 to 1296)
  AUTHORS   Thompson,D.E., Brehm,J.K., Oultram,J.D., Swinfield,T.J.,
            Shone,C.C., Atkinson,T., Melling,J. and Minton,N.P.
  TITLE     The complete amino acid sequence of the Clostridium botulinum type
            A neurotoxin, deduced by nucleotide sequence analysis of the
            encoding gene
  JOURNAL   Eur. J. Biochem. 189 (1), 73-81 (1990)
  MEDLINE   90235864
   PUBMED   2185020
  REMARK    SEQUENCE FROM N.A.
            STRAIN=NCTC 2916
REFERENCE   2  (residues 1 to 1296)
  AUTHORS   Binz,T., Kurazono,H., Wille,M., Frevert,J., Wernars,K. and
            Niemann,H.
  TITLE     The complete sequence of botulinum neurotoxin type A and comparison
            with other clostridial neurotoxins
  JOURNAL   J. Biol. Chem. 265 (16), 9153-9158 (1990)
  MEDLINE   90264400
   PUBMED   2160960
  REMARK    SEQUENCE FROM N.A.
            STRAIN=62A
REFERENCE   3  (residues 1 to 1296)
  AUTHORS   East,A.K., Bhandari,M., Stacey,J.M., Campbell,K.D. and Collins,M.D.
  TITLE     Organization and phylogenetic interrelationships of genes encoding
            components of the botulinum toxin complex in proteolytic
            Clostridium botulinum types A, B, and F: evidence of chimeric
            sequences in the gene encoding the nontoxic nonhemagglutinin
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component
JOURNAL Int. J. Syst. Bacteriol. 46 (4), 1105-1112 (1996)
MEDLINE 97016817
PUBMED 8863443
REMARK SEQUENCE OF 1-65 FROM N.A.
STRAIN=62A
REFERENCE 4 (residues 1 to 1296)
AUTHORS Betley,M.J., Somers,E. and DasGupta,B.R.
TITLE Characterization of botulinum type A neurotoxin gene: delineation of the N-terminal encoding region
JOURNAL Biochem. Biophys. Res. Commun. 162 (3), 1388-1395 (1989)
MEDLINE 89350959
PUBMED 2669749
REMARK SEQUENCE OF 1-34 FROM N.A.
STRAIN=Hall
REFERENCE 5 (residues 1 to 1296)
AUTHORS Fujita,R., Fujinaga,Y., Inoue,K., Nakajima,H., Kumon,H. and Oguma,K.
TITLE Molecular characterization of two forms of nontoxic-nonhemagglutinin components of Clostridium botulinum type A progenitor toxins
JOURNAL FEBS Lett. 376 (1-2), 41-44 (1995)
MEDLINE 96096783
PUBMED 8521962
REMARK SEQUENCE OF 1-18 FROM N.A.
STRAIN=Type A NIH
REFERENCE 6 (residues 1 to 1296)
AUTHORS Schmidt,J.J., Sathyamoorthy,V. and DasGupta,B.R.
TITLE Partial amino acid sequence of the heavy and light chains of botulinum neurotoxin type A
JOURNAL Biochem. Biophys. Res. Commun. 119 (3), 900-904 (1984)
MEDLINE 84178501
PUBMED 6370252
REMARK SEQUENCE OF 1-16.
REFERENCE 7 (residues 1 to 1296)
AUTHORS Dasgupta,B.R., Foley,J. and Niece,R.
TITLE Partial sequence of the light chain of botulinum neurotoxin type A
JOURNAL Biochemistry 26, 4162-4162 (1987)
REMARK SEQUENCE OF 1-46.
REFERENCE 8 (residues 1 to 1296)
AUTHORS DasGupta,B.R. and Dekleva,M.L.
TITLE Botulinum neurotoxin type A: sequence of amino acids at the N-terminus and around the nicking site
JOURNAL Biochimie 72 (9), 661-664 (1990)
MEDLINE 91120847
PUBMED 2126206
REMARK SEQUENCE OF 1-5 AND 444-456.
REFERENCE 9 (residues 1 to 1296)
AUTHORS Sathyamoorthy,V., Dasgupta,B.R., Foley,J. and Niece,R.L.
TITLE Botulinum neurotoxin type A: cleavage of the heavy chain into two halves and their partial sequences
JOURNAL Arch. Biochem. Biophys. 266 (1), 142-151 (1988)
MEDLINE 89024662
PUBMED 3178218
REMARK SEQUENCE OF 448-464 AND 872-895.
REFERENCE 10 (residues 1 to 1296)
AUTHORS Shone,C.C., Hambleton,P. and Melling,J.
TITLE Inactivation of Clostridium botulinum type A neurotoxin by trypsin and purification of two tryptic fragments. Proteolytic action near the COOH-terminus of the heavy subunit destroys toxin-binding activity
JOURNAL Eur. J. Biochem. 151 (1), 75-82 (1985)
MEDLINE 85285016
PUBMED 3896784
REMARK SEQUENCE OF 448-482.

[redacted]

REFERENCE 11 (residues 1 to 1296)
AUTHORS Schiavo,G., Santucci,A., Dasgupta,B.R., Mehta,P.P., Jontes,J., Benfenati,F., Wilson,M.C. and Montecucco,C.
TITLE Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds
JOURNAL FEBS Lett. 335 (1), 99-103 (1993)
MEDLINE 94063091
PUBMED 8243676
REMARK IDENTIFICATION OF SUBSTRATE.
REFERENCE 12 (residues 1 to 1296)
AUTHORS Binz,T., Blasi,J., Yamasaki,S., Baumeister,A., Link,E., Sudhof,T.C., Jahn,R. and Niemann,H.
TITLE Proteolysis of SNAP-25 by types E and A botulinal neurotoxins
JOURNAL J. Biol. Chem. 269 (3), 1617-1620 (1994)
MEDLINE 94124495
PUBMED 8294407
REMARK IDENTIFICATION OF SUBSTRATE.
REFERENCE 13 (residues 1 to 1296)
AUTHORS Rigoni,M., Caccin,P., Johnson,E.A., Montecucco,C. and Rossetto,O.
TITLE Site-directed mutagenesis identifies active-site residues of the light chain of botulinum neurotoxin type A
JOURNAL Biochem. Biophys. Res. Commun. 288 (5), 1231-1237 (2001)
MEDLINE 21556941
PUBMED 11700044
REMARK MUTAGENESIS OF GLU-261; PHE-265 AND TYR-365.
REFERENCE 14 (residues 1 to 1296)
AUTHORS Lacy,D.B., Tepp,W., Cohen,A.C., DasGupta,B.R. and Stevens,R.C.
TITLE Crystal structure of botulinum neurotoxin type A and implications for toxicity
JOURNAL Nat. Struct. Biol. 5 (10), 898-902 (1998)
MEDLINE 98455071
PUBMED 9783750
REMARK X-RAY CRYSTALLOGRAPHY (3.3 ANGSTROMS).
COMMENT On or before Sep 14, 1993 this sequence version replaced gi:115193, gi:115174.

[FUNCTION] Inhibits acetylcholine release. The botulinum toxin binds with high affinity to peripheral neuronal presynaptic membrane, is then internalized by receptor-mediated endocytosis. The C-terminus of the heavy chain (H) is responsible for the adherence of the toxin to the cell surface while the N-terminus mediates transport of the light chain from the endocytic vesicle to the cytosol. After translocation, the light chain (L) hydrolyzes the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking neurotransmitter release. Inhibition of acetylcholine release results in flaccid paralysis, with frequent heart or respiratory failure.
[CATALYTIC ACTIVITY] Limited hydrolysis of proteins of the neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No detected action on small molecule substrates.
[SUBUNIT] Disulfide-linked heterodimer of a light chain (L) and a heavy chain (H).
[SUBCELLULAR LOCATION] Secreted.
PHARMACEUTICAL: Available under the name BOTOX (Allergan) for the treatment of strabismus and blepharospasm associated with dystonia and cervical dystonia. Also used for the treatment of hemifacial spasm and a number of other neurological disorders characterized by abnormal muscle contraction.
[MISCELLANEOUS] There are seven antigenically distinct forms of

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            botulinum neurotoxin: Types A, B, C1, D, E, F, and G.
            [SIMILARITY] BELONGS TO PEPTIDASE FAMILY M27.
            [DATABASE] NAME=BOTOX product information Web site;
            WWW='http://www.botox.com/index.jsp?hp&productinfo".
            [DATABASE] NAME=Protein Spotlight; NOTE=Issue 19 of February 2002;
            WWW='http://www.expasy.org/spotlight/articles/sptlt019.html".
FEATURES            Location/Qualifiers
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                    /note="BNA; ATX"
     Protein        1..1296
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                    /EC_number="3.4.24.69"
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                    /region_name="Mature chain"
                    /note="BOTULINUM NEUROTOXIN A, LIGHT-CHAIN."
     Region         2
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                    /region_name="Conflict"
                    /note="P -> Q (IN REF. 1)."
     Region         27
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                    /region_name="Variant"
                    /note="V -> A."
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                    /note="ZINC (CATALYTIC)."
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                    /note="ZINC (CATALYTIC)."
     Site           262
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                    /site_type="mutagenized"
                    /note="E->A: DRASTIC DECREASE IN ENZYMATIC ACTIVITY."
     Site           266
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                    /site_type="mutagenized"
                    /note="F->A: DECREASE IN ENZYMATIC ACTIVITY."
     Site           366
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                    /site_type="mutagenized"
                    /note="Y->A: DECREASE IN ENZYMATIC ACTIVITY."
     Bond           bond(430,454)
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                    /bond_type="disulfide"
                    /note="INTERCHAIN."
     Region         449..1296
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                    /region_name="Mature chain"
                    /note="BOTULINUM NEUROTOXIN A, HEAVY-CHAIN."
     Region         480
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[redacted]

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                     /note="E -> P (IN REF. 9)."
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                     /note="POTENTIAL."
     Region          656..676
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                     /region_name="Transmembrane region"
                     /note="POTENTIAL."
     Region          876
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                     /region_name="Conflict"
                     /note="T -> L (IN REF. 8)."
     Region          892
                     /gene="BOTA"
                     /region_name="Conflict"
                     /note="S -> K (IN REF. 8)."
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      121 stidtelkvi dtncinviqp dgsyrseeln lviigpsadi iqfecksfgh evlnltrngy
      181 gstqyirfsp dftfgfeesl evdtnpllga gkfatdpavt lahelihagh rlygiainpn
      241 rvfkvntnay yemsglevsf eelrtfgghd akfidslqen efrlyyynkf kdiastlnka
      301 ksivgttasl qymknvfkek yllsedtsgk fsvdklkfdk lykmlteiyt ednfvkffkv
      361 lnrktylnfd kavfkinivp kvnytiydgf nlrntnlaan fngqnteinn mnftklknft
      421 glfefykllc vrgiitsktk sldkgynkal ndlcikvnnw dlffspsedn ftndlnkgee
      481 itsdtnieaa eenisldliq qyyltfnfdn epenisienl ssdiigqlel mpnierfpng
      541 kkyeldkytm fhylraqefe hgksrialtn svneallnps rvytffssdy vkkvnkatea
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     1021 nnrlnnskiy ingrlidqkp isnlgnihas nnimfkldgc rdthryiwik yfnlfdkeln
     1081 ekeikdlydn qsnsgilkdf wgdylqydkp yymlnlydpn kyvdvnnvgi rgymylkgpr
     1141 gsvmttniyl nsslyrgtkf iikkyasgnk dnivrnndrv yinvvvknke yrlatnasqa
     1201 gvekilsale ipdvgnlsqv vvmksknqqg itnkckmnlq dnngndigfi gfhqfnniak
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Revised: July 5, 2002.

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ID   Q57236      PRELIMINARY;      PRT;  1278 AA.
AC   Q57236; Q45863;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Botulinum neurotoxin type F (BONT/F protein).
GN   BONT/F.
OS   Clostridium botulinum.
OC   Bacteria; Firmicutes; Bacillus/Clostridium group; Clostridia;
OC   Clostridiales; Clostridiaceae; Clostridium.
OX   NCBI_TaxID=1491;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=NCTC 10281;
RA   Hutson R.A., Collins M.D.;
RL   Submitted (AUG-1995) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Elmore M.J., Bodsworth N.J., Whelan S.M., Minton N.P.;
RL   Submitted (AUG-1994) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE OF 635-1000 FROM N.A.
RC   STRAIN=NCTC 1028;
RX   MEDLINE=94013372; PubMed=8408542;
RA   Campbell K., East A.K., Collins M.D.;
RT   "Gene probes for identification of the botulinal neurotoxin gene and
RT   specific identification of neurotoxin types B, E, and F.";
RL   J. Clin. Microbiol. 31:2255-2262(1993).
RN   [4]
RP   SEQUENCE OF 1-27 FROM N.A.
RC   STRAIN=LANGELAND;
RX   MEDLINE=98404102; PubMed=9732534;
RA   East A.K., Bhandari M., Hielm S., Collins M.D.;
RT   "Analysis of the botulinum neurotoxin type F gene clusters in
RT   proteolytic and nonproteolytic Clostridium botulinum and Clostridium
RT   barati.";
RL   Curr. Microbiol. 37:262-268(1998).
DR   EMBL; X81714; CAA57358.1; -.
DR   EMBL; L35496; AAA23210.1; -.
DR   EMBL; X70821; CAA50152.1; -.
DR   EMBL; X99064; CAA67512.1; -.
DR   HSSP; P10845; 3BTA.
DR   MEROPS; M27.002; -.
DR   InterPro; IPR000395; Bontoxilysin.
DR   InterPro; IPR006025; Zn_MTpeptdse.
DR   Pfam; PF01742; Peptidase_M27; 1.
DR   PRINTS; PR00760; BONTOXILYSIN.
DR   ProDom; PD001963; Bontoxilysin; 1.
DR   PROSITE; PS00142; ZINC_PROTEASE; UNKNOWN_1.
KW   Neurotoxin.
SQ   SEQUENCE   1278 AA;  147073 MW;  A1BE1318431D6918 CRC64;
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     EHTPINEFHP VTRTTSVNIK SSTNVKSSII LNLLVLGAGP DIFENSSYPV RKLMDSGGVY
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     NNYRNNLDEV ILDYNSETIP QISNQTLNTL VQDDSYVPRY DSNGTSEIEE HNVVDLNVFF
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[redacted]

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